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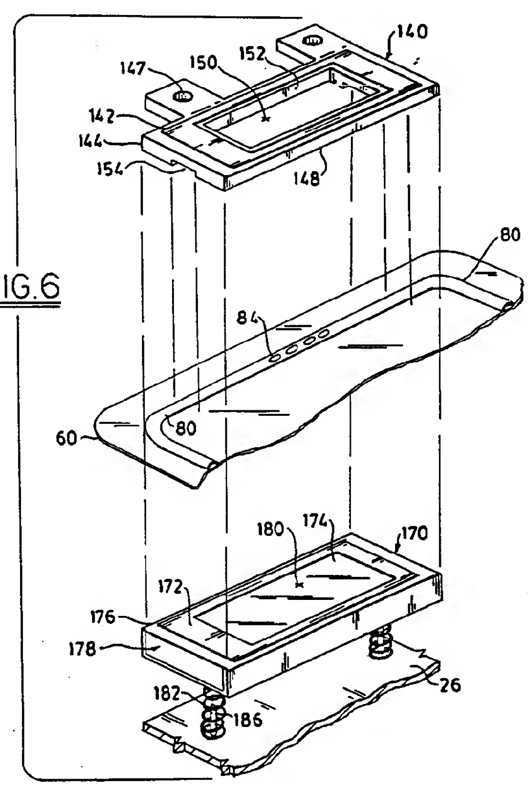
(54) Apparatus for heating a fluid-carrying compartment of a reaction cuvette.

(57) A heating assembly (20) useful in apparatus for processing reaction cuvettes for replicating specified DNA sequences, such as those using PCR, having a heating element (140) with a heat delivering surface for compressively contacting a pliable fluid-carrying compartment (80,84) of a supported cuvette. The heat delivering surface has a defined passage (154) sized to allow the detection compartment (84) to be situated therein so that the compartment (84) can be efficiently heated. Fluid flow through the compartment (84), however, is not interfered with during the heating process due to the presence of the defined passage (154). In addition, the heat delivering surface can be made from optically transparent materials (150) so that visual detection within the processor can take place.

FIG.6



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The invention is directed to apparatus for the processing of reaction cuvettes, such as for amplification and detection of specific nucleic acid sequences, and in particular to the mounting of heating assemblies to heat by contact a fluid-carrying compartment of such cuvettes.

Self contained reaction cuvettes are known and described, such as in EPA Publication No. 0/381,501, in which amplification of specified nucleic acids, such as a DNA sequence(s) can take place by means of polymerase chain reaction technology (hereinafter PCR). The cuvettes are self-contained such that a sample can be introduced within its confines, the cuvettes having separate reaction, reagent and detection compartments so that amplification, wash and detection can be performed. The individual compartments of the reaction cuvette are preferably thin walled and made from a pliable material which is preferably transparent. Within the detection compartment of a typical reaction cuvette, controls or other detection means are located within or added to the pliable, see-through compartment.

In order to effectively conduct the amplification process, including the detection of replicated nucleic acid, such as DNA, it is important to heat the detection compartment as well as other portions of the cuvette. Efficient heating, such as by conduction, requires that heating elements be placed in direct compressive contact with the reaction cuvette. It is also essential, however, that fluid communication into and out of the detection compartment is not constricted so that liquid will be able to contact the detection controls located therein, as well as having the ability to flow out into adjacent compartments, such as for the collection of waste products.

Therefore, there is a problem of providing a heating assembly which will effectively heat by contact a fluid-carrying compartment of a reaction cuvette, such as those described, while also allowing fluid flow to proceed through the compartment.

The present invention solves the above stated problem by providing an assembly for heating a fluid-carrying portion of a reaction cuvette comprising:

a first heating element comprising a source of heat and a heat-delivering surface;

a support for supporting a reaction cuvette having at least one compliant fluid-carrying compartment;

and means for moving the heat-delivering surface into and out of intimate contact with a portion of the supported cuvette,

characterized in that wherein the heat-delivering surface further comprises means defining a fixed passage permanently sized to receive the at least one compliant fluid-carrying compartment for allowing flow therethrough while the first heating element is engaged with the cuvette.

According to another aspect of the present invention, the problem is solved by a processing apparatus comprising:

a main body having an interior portion;

a cover movably attached to the main body;

a support for supporting a reaction cuvette disposed within the interior portion, the cuvette having at least one compliant fluid-carrying compartment;

a first heating element having a source of heat and a first heat-delivering surface capable of heating the reaction cuvette by contact therewith, the first heating element having means defining a fixed passage permanently sized to receive the fluid-carrying compartment for permitting fluid flow therethrough while the first heating element is in contact with the reaction cuvette; and

means for moving the first heating element into intimate contact with a supported reaction cuvette.

An advantageous feature realized by the present invention is that a reaction cuvette, useful for nucleic acid amplification, can be placed within a processor so that a detection compartment of the cuvette can be brought into intimate thermal contact with the heat delivering surface so as to promote efficient heating of the compartment, while still permitting fluid flow to proceed into and out of the compartment.

Another advantageous feature of a processor having the heating assembly according to the present invention is that the results of the reaction can be observed without having to open the processor, and without having to interfere with the amplification or detection aspects of the process.

Other advantageous features will become apparent upon reference to the following Description of the Preferred Embodiments, when read in light of the attached drawings, wherein:

FIG. 1 is a frontal perspective view of a processing apparatus according to one embodiment of the present invention.

FIG. 2 is a top plan view of a reaction cuvette which is useful in the processor shown in FIG. 1.

FIG. 3 is a fragmented side elevational view, partially sectioned, of the processor shown in FIG. 1, particularly showing the relationship between the cover of the processor and a support plate located therein.

FIG. 4 is a partial top plan view of the processor of FIG. 3.

FIG. 5 is a fragmented side elevational view, partially shown in section, of the processor of FIGS. 3 and 4.

FIG. 6 is an exploded perspective view of portions of an upper and lower heating assembly according to the present invention in relation to the reaction cuvette of FIG. 2.

FIG. 7 is a partial side elevational view of the processor of FIG. 1, shown in section, illustrating the engagement of the heating assemblies of FIG. 6 while the cover of the processor is closed.

FIG. 8 is a partial side elevational view of the

processor of FIG. 7, shown in section, illustrating the engagement of the two heating assemblies after the cover of the processor has been opened.

FIG. 9 is an enlarged sectional view of the portion of FIG. 7 identified as IX.

FIG. 10 is a partial side elevational view, shown in section, of an alternate embodiment for engaging and heating a compartment of the reaction cuvette.

The invention is hereinafter described in the context of the preferred embodiments.

Terms such as "up", "down", "lower", "vertical", "horizontal", and 'bottom" as used herein refer to the orientation of parts when the apparatus is positioned in its customary position of use.

Referring to FIG. 1, there is provided a processor 20 for performing DNA replication through the use of PCR (polymerase chain reaction) technology of a plurality of reaction cuvettes 60, the apparatus having a cover 30, a movable support plate 40 for supporting the plurality of reaction cuvettes 60, and upper and lower heating assemblies 140, 170, for heating a fluid-carrying portion of each supported cuvette 60.

Prior to a detailed discussion of the general workings of processor 20, and in particular heating assemblies 140, 170, it is important to understand the structure and operation of a typical PCR reaction cuvette 60. A particular configuration of a reaction cuvette 60 is illustrated in FIG. 2. Cuvette 60 is defined as a self-contained pouch having a reaction compartment 62 and adjacent storage compartments 64, 66, 68. Inlet means 70, 72 allow a sample and reagents for promoting the amplification process to be added to reaction chamber 62, though the reagents could already be preincorporated therein. All of the compartments are interconnected by a network of flow passageways 74, 76, 78, 80 which lead sequentially to a detection compartment 84. Flow passageway 80 extends from the other side of detection compartment 84 to a waste chamber 86.

As noted previously, the entire cuvette 60 is self-contained and is formed by heat-sealing two thin-walled plastic sheets 88, 90 together at their respective side edges. Details of the manufacture of the described cuvettes are described in EPA Publication No. 0/550,090.

Nucleic acid amplification, in general, is done by the introduction of sample into reaction compartment 62 via inlet means 70, 72 into which reagents are also added, or are already preincorporated. These inlet means 70, 72 are then permanently closed off to preserve the self-contained nature of the cuvette. Typically, the inlet means are heat-sealed after introduction of sample. These reagents, in combination with thermal cycling of reaction compartment 62 allow denaturing of the DNA or other nucleic acid strands and subsequent replication to produce amplified nucleic acid. Once the desired amount of nucleic acid material has been produced within chamber 62, external pressure can then be applied to force the contents of chamber 62 along flow passageway 74 and towards detection compartment 84. Sequentially, the pressurizing of adjacent storage compartments 64, 66, 68, according to a particular protocol, force wash liquid and detection reagents from their respective compartments to traverse flow passageways 76, 78 and 80 so that their contents may be added to detection compartment 84 which already contains means for immobilizing amplified nucleic acid for detection therein. Excess liquid is forced from detection compartment 84 to adjacent waste compartment 86. With the possible exception of the introduction of sample the entire process, including detection, can be completed without having to open cuvette 60, thereby avoiding aerosoling problems which could contaminate a laboratory environment. Details of the processing of cuvettes 60, including detection, can be found in EPA Publication No. 0/381,501.

Referring to FIGS. 3-5, the general workings of processor 20 will now be described. Cover 30 is movably attached to the main body 22 of processor 20 so that it can open and close as per arrow 32, FIG. 5, thereby allowing operator access to an interior portion, for loading and unloading of cuvettes 60. Preferably, cover 30 is made from a lightweight, transparent material to allow user viewing. In the embodiment illustrated, cover 30 is made from polycarbonate, and main body 22 is made of polycarbonate, though other conventional structural materials, such as polyesters, polyamides, polyurethanes, polyolefins, polyacetals, phenol-formaldehyde resins, and so forth, can be used.

Disposed within the interior portion is a support plate 40, sized to receive at least one PCR pouch or cuvette 60 of the type previously described above. In the embodiment illustrated, support plate 40 is sized to hold a plurality of reaction cuvettes 60 to be placed along a top surface 42, the cuvettes 60 being generally parallel and equally spaced apart with respect to one another when they are loaded. When cover 30 is closed, support plate 40 is initially in an inclined first position (A). When cover 30 is closed, as in the embodiment illustrated, support plate 40 is inclined approximately 19 degrees from horizontal, FIG. 3. The specified angle of inclination of position (A), however, is not critical to the operation of the present invention, but is preferable for ease of loading and unloading of cuvettes 60, as is discussed in greater detail below.

Support plate 40 is movably attached to cover 30 by camming means comprising a rotatable cam shaft 52 having a plurality of cam surfaces 54 extending therefrom, shaft 52 being positioned beneath support plate 40. Shaft 52 is connected at one end along one side of processor 20 by a movable lower linkage 56 which is pinned or otherwise attached to a pivot arm 58 extending to an upper linkage 59 which is connect-

ed to one side of cover 30. A set of bearings (not shown) enables smooth, repeatable rotation of cam shaft 52.

The operation of camming means 50 can be seen by also referring to FIGS. 3-5. As cover 30 is opened, FIG. 5, per arrow 32, cam shaft 52 is rotated in a counterclockwise fashion, as shown, thereby engaging cam surfaces 54, FIG. 4, against the bottom of support plate 40, and relocating support plate 40 to substantially horizontal position (B) in which reaction cuvettes 60, FIG. 2, as previously described, can more easily be loaded. In like manner, when cover 30 is closed, cam shaft 52 reverses direction and returns support plate 40 to initial position (A), FIG. 3. In a preferential embodiment, an extension spring (not shown) can be added to cover 30 which is loaded upon opening and provides uniformity in registering cam surfaces 54 when cover 30 is closed.

Processor 20 is also provided with a translatable roller arm 28 which can be engaged per arrow 34 against support plate top surface 42. Roller arm 28 is guided by control means, such as a microprocessor (not shown), and is driven by a servo motor and a belt mechanism (not shown) to engage a loaded cuvette 60, FIG. 2, by means of a series of retractable rollers 29 extending from the bottom surface of roller arm 28 for compressing sequentially the reaction compartment 62 and storage compartments 64, 66, 68 of a plurality of loaded cuvettes.

It can be seen that roller arm 28 can freely move along top surface 42 when support plate 40 is in position (A), FIG. 3, but is not free to engage support plate when cuvettes are being loaded in position (B), FIG. 5.

Referring to FIGS. 1 and 6, an upper and lower detection heater assembly 140 and 170, respectively are each provided for engaging the detection compartment 84 and flow passageways 80 of a reaction cuvette 60.

Upper heater assembly 140 comprises a first heating element 142, such as a thin electrically resistive member, which is bonded to one side of an aluminum or other thermally conductive support or mount fixture 144. Heating element 142 is further preferably defined by a peripheral configuration about a through aperture 150 provided in mount fixture 144, and sized to receive the detection compartment 84 of a reaction cuvette 60, when aligned according to FIG. 6. Aperture 150 cooperates with transparent processor cover 30 to permit visual inspection of detection compartment 84 without interfering with the heating thereof.

Due to the thermally conductive nature of mount fixture 144, heat can be transmitted through inner sidewalls 152, as well as through lower surface 148, thereby defining a first heat delivering surface for assembly 140 to heat by contact a reaction cuvette 60.

Lower surface 148 is further defined by a channel or passage 154, preferably sized to receive flow passageway 80 on either side of detection compartment 84. Channel 154 extends across the length of heat-delivering surface 148, except for aperture 150, and provides for a recessed area so that any downward compressive force exerted by mount fixture 144 is transmitted by the remainder of lower surface 148, to portions of the surface area of cuvette 60, but not to the fluid-carrying portions defined by detection compartment 84 and flow passageways 80.

Still referring to FIG. 6, a second or lower heating assembly 170 is provided for contacting the underside of reaction cuvette 60 in the vicinity of detection compartment 84. Lower heating assembly 170 comprises a second heating element 172, such as an electrically resistive member which is bonded to an exterior surface of a glass, or preferably other optically transparent member 174, such as sapphire. A holding fixture or button 176, retains glass member 174 and heating element 172 in a holding aperture 178, sized so that glass member 174 is fully contained therein, preferably such that the exterior surface of glass member 174 is substantially flush with the open periphery of button 176.

A pair of compression springs 182 are provided between the bottom surface of button 176 and a stationary weldment 26, of processor 20 which is located beneath support plate 40, FIG. 7, and which spans the interior portion of processor 20, springs 182 being supported via a set of shoulder screws 186. It can be seen from FIGS. 3, 5 that as support plate 40 is made to move from position (A) to position (B), lower heating assembly 170 essentially remains fixed.

Thin heating element 172 is defined by a similar peripheral edge configuration as upper assembly 140 to enclose a substantially central see-through portion, or window 180 of glass member 174 which is sized to fit detection compartment 84. A similar window (not shown) is provided along the bottom surface of button 176 to permit an optical path for detection compartment 84, such as by machine means (not shown).

In the embodiment illustrated, a series of second heating assemblies 170 are provided in processor 20. Sources of heat necessary to engage heating elements 142, 172, such as a resistive coil, are not shown, but such heat sources are commonly known.

Turning to FIG. 7 and 8, details of the upper and lower heating assemblies in combination with each other and the remainder of processor 20 will now be described. Adjacent top surface 42 of support plate 40 is a flip-up plate 146 to which upper heating assembly 140; that is, mount fixture 144 and heating element 142, can be mounted via mount holes 147, FIG. 6, configured as shown, and through which threaded fasteners can be inserted. Flip-up plate 146 can be made to selectively open or close by a catch mechanism 156 which engages plate 146. A torsion spring

(not shown) holds plate 146 open when catch mechanism 156 is disengaged. An aperture 158 is provided for flip-up plate 146 which is coincident with aperture 150, FIG. 6, when placed in a closed position, FIG. 7.

Turning to the lower heating assembly, button 176 is loosely positioned within a retaining plate 184 which as shown, FIGS. 7 and 8, is mounted to stationary weldment 26.

A series of equally spaced parallel apertures 46, are provided through the thickness of support plate 40, each being sized for receiving a second heating assembly 170 when support plate 40 is moved from loading position (B), to initially inclined position (A). The entire lower heating assembly 170, including stationary weldment 26, is inclined so that the assembly will fit within aperture 46 when support plate 40 is restored to position (A). In a preferable orientation, the exterior surface 188 of retaining plate 184 and top surface 42 are substantially flush to one another when support plate 40 is placed in position (A), while button 176 extends a small distance above top surface 42. The entire lower heating assembly, including retaining plate 184, is thereafter rigid with the exception of button 176 which is movable along axis 190, FIG. 7, due to the resiliency of springs 182 bearing against the bottom of button 176 and weldment 26 respectively.

In operation and referring to FIGS. 1-9, when processor cover 30 is opened, support plate 40 is caused to move from initial inclined position (A) to a substantially horizontal loading position (B) due to the connected interaction between cover 30 and camming means 50, in which cam shaft 52 is rotated, thereby bringing camming surfaces 54 into contact with the bottom of support plate 40. As previously noted, roller arm 28 cannot be engaged while support plate is in position (B).

A plurality of reaction cuvettes 60 can then be loaded on top surface 42 into a series of defined slots (not shown), the compartments of each cuvette 60 facing upward, or oppositely situated away, from top surface 42. Flip-up plate 146 is preferably closed during loading, as shown in FIG. 8. Cuvettes 60 are held loosely on top surface 42, until upper heating assembly 140 is brought into contact therewith. Each cuvette 60 is properly aligned during loading so that the underside of each detection compartment 84 is coincident with a defined aperture 46 to insure alignment with lower heating assembly 170 when support plate 40 is relocated to position (B).

Upper heating assembly 140 is brought into contact with detection compartment 84 by swinging support plate 40 downward so that detection compartment 84 is within aperture 150 and flow passageways 80 on either side of detection compartment 84 are within channel 154. Each flip-up plate 146 is normally locked into place by the engagement of catch 156 which effectively places lower surface 148 in substantial thermal contact with cuvette 60.

Once reaction cuvettes 60 are placed on support plate 40, and upper heating assembly 140 has been positioned as described above, processor cover 30 can be closed, FIG. 7, thereby relocating support plate 40 and reaction cuvettes 60 to initial position (A). This position lowers support plate 40 adjacent stationary weldment 26 and particularly to lower heating assemblies 170. Since the top surface of button 176 preferably extends above support plate top surface 42, the added thickness of each reaction cuvette 60, loads springs 182 thereby placing both upper and lower heating assemblies 140, 170 into compressive and intimate thermal contact with reaction cuvette 60. As noted previously, however, channel 154, FIG. 9, having sufficient clearance for flow passageways 80, however, does not interfere with fluid communication to and from detection compartment 84 while significant thermal contact has been achieved between upper and lower heater assemblies 140, 170, FIG. 6, and cuvettes 60.

Most preferably, surface 200 of channel 154 is configured and spaced from the surface of window 180, FIG. 9, so that surface 200 acts to constrain the amount of expansion that occurs in compartment 80. As a result, within the range of expected pressures that occur in that compartment, there will be a predicted expansion and volume of flow-through liquid. In addition, flow characteristics at edges 202 of the compartment will be uniform. A useful spacing h between surface 200 and the exterior surface of window 180 to provide this effect is 0.3 mm.

Alternately, the upper and lower heating assemblies 140, 170, shown in FIG. 6, can be replaced, see FIG. 10, by providing lower and upper constraint plates 210, 220 positioned-in recessed portions which are provided in support plate 40 and flip up plate 146 respectively. Plates 210, 220 are made from a thermally conductive, transparent material, such as glass or sapphire, so that a detection compartment 84 sandwiched between the plates can be optically viewed as previously described. A heating element (not shown) is bonded to each constraint plate 210, 220 in a manner which is conventionally known.

Support plate 40 is milled so that. the recessed portion for fitting lower constraint plate 210 defines a predetermined spacing h_1 between the top surface 212 of lower constraint plate 210 and the bottom surface 222 of upper constraint plate 220. For a cuvette having wall thicknesses of 0.1 mm, a spacing of 0.3 mm is particularly useful.

In operation, when a cuvette 60 is introduced into the apparatus as shown and fluid is introduced into detection compartment 84, plates 210 and 220 permit an inflation of approximately 0.1 mm before restricting the compartment from further expansion. This allows fluid to pass through the compartment and with

a relatively constant flow profile. Because plates 146 and 40 are held in compressive contact by catch mechanism 156, intimate thermal contact is insured between the heat delivering surfaces of plates 210, 220 and detection compartment 84. In this way, both enhanced fluid flow and adequate heating of cuvette 60 are accomplished and without requiring a spring loaded mechanism.

It should be readily apparent that spacing h, can be varied depending largely upon the volume and viscosity of fluid contained within the cuvette, wall thickness and pliability of wall material as well as other determinative factors.

Reading of a color change occurring in any one of the dots in compartment 84, FIG. 2, is done by a reflectometer, which can be conventional (not shown).

In addition, by providing apertures 46, detection compartment 84 can be viewed without having to open cover 30, or by otherwise interrupting the amplification process.

Claims

1. An assembly for heating a fluid-carrying portion of a reaction cuvette comprising:
   a first heating element comprising a source of heat and a heat-delivering surface;
   a support for supporting a reaction cuvette having at least one compliant fluid-carrying compartment;
   and means for moving the heat-delivering surface into and out of intimate contact with a portion of the supported cuvette,
   characterized in that the heat-delivering surface further comprises means defining a fixed passage permanently sized to receive the at least one compliant fluid-carrying compartment for allowing flow therethrough while the first heating element is engaged with the cuvette.

2. An assembly as claimed in 1 further comprising means for viewing the fluid-carrying compartment while the first heating element is engaged with the cuvette.

3. An assembly as claimed in 1 wherein the first heating element is made from an optically transparent material.

4. An assembly as claimed in 1 further comprising a second heating element having a source of heat and a heat-delivering surface, wherein the supported cuvette is positioned between the first and the second heat-delivering surfaces, the assembly further comprising means for moving at least one of the heating elements relative to the reaction cuvette and into and out of engagement therewith.

5. An assembly as claimed in claim 5 further comprising means for resiliently biasing the heating elements into contact with the supported cuvette.

6. An assembly as claimed in claim 4 wherein the second heating element is made from an optically transparent material.

7. An assembly as claimed in 1 wherein the first heating element further comprises means defining an aperture extending through the element and sized to receive the fluid-carrying compartment.

8. An assembly as claimed in claim 1 wherein the first heating element is movably connected to the support for moving the heat-delivering surface into and out of contact with the cuvette.

9. An assembly as defined in claim 1, wherein the passage is sized to constrain expansion of the fluid-carrying compartment by pressing against it when fluid pressure is present.

10. A processing apparatus comprising:
    a main body having an interior portion;
    a cover movably attached to the main body;
    a support for supporting a reaction cuvette disposed within the interior portion, the cuvette having at least one compliant fluid-carrying compartment;
    a first heating element having a source of heat and a first heat-delivering surface capable of heating the reaction cuvette by contact therewith, the first heating element having means defining a fixed passage permanently sized to receive the fluid-carrying compartment for permitting fluid flow therethrough while the first heating element is in contact with the reaction cuvette; and
    means for moving the first heating element into intimate contact with a supported reaction cuvette.

11. A processing apparatus as claimed in claim 10 further comprising means for viewing the fluid-carrying compartment when the first heating element is engaged with the reaction cuvette.

12. A processing apparatus as claimed in claim 11 wherein the first heating element is made from an optically transparent material.

13. A processing apparatus as claimed in claim 11

wherein the first heating element has means defining an aperture for viewing the fluid-carrying compartment.

14. A processing apparatus as claimed in claim 10 wherein the support is movable from a first to a second position and is coupled by means to the cover so that the support moves from the first position to the second position when the cover is opened.

15. A processing apparatus as claimed in claim 10 further comprising a second heating element having a source of heat and a heat-delivering surface for heating by contact the reaction cuvette.

16. A processing apparatus as claimed in claim 14 wherein the support further comprises means defining an aperture sized to receive the second heating element when the support is moved from the second to the first position.

17. A processing apparatus as claimed in claim 15 further comprising means for resiliently biasing the second heating element so as to compressively contact the test element when the support is moved from the second to the first position.

18. A processing apparatus as claimed in 15 wherein the second heating element is made from an optically transparent material.

19. A processing apparatus as claimed in claim 14 and further comprising means for moving the first heating element into and out of contact with the portion of the reaction cuvette, the means being coupled to the support.

20. A processing apparatus as claimed in claim 11 further comprising means for detecting the presence of at least one substance in the fluid-carrying compartment.

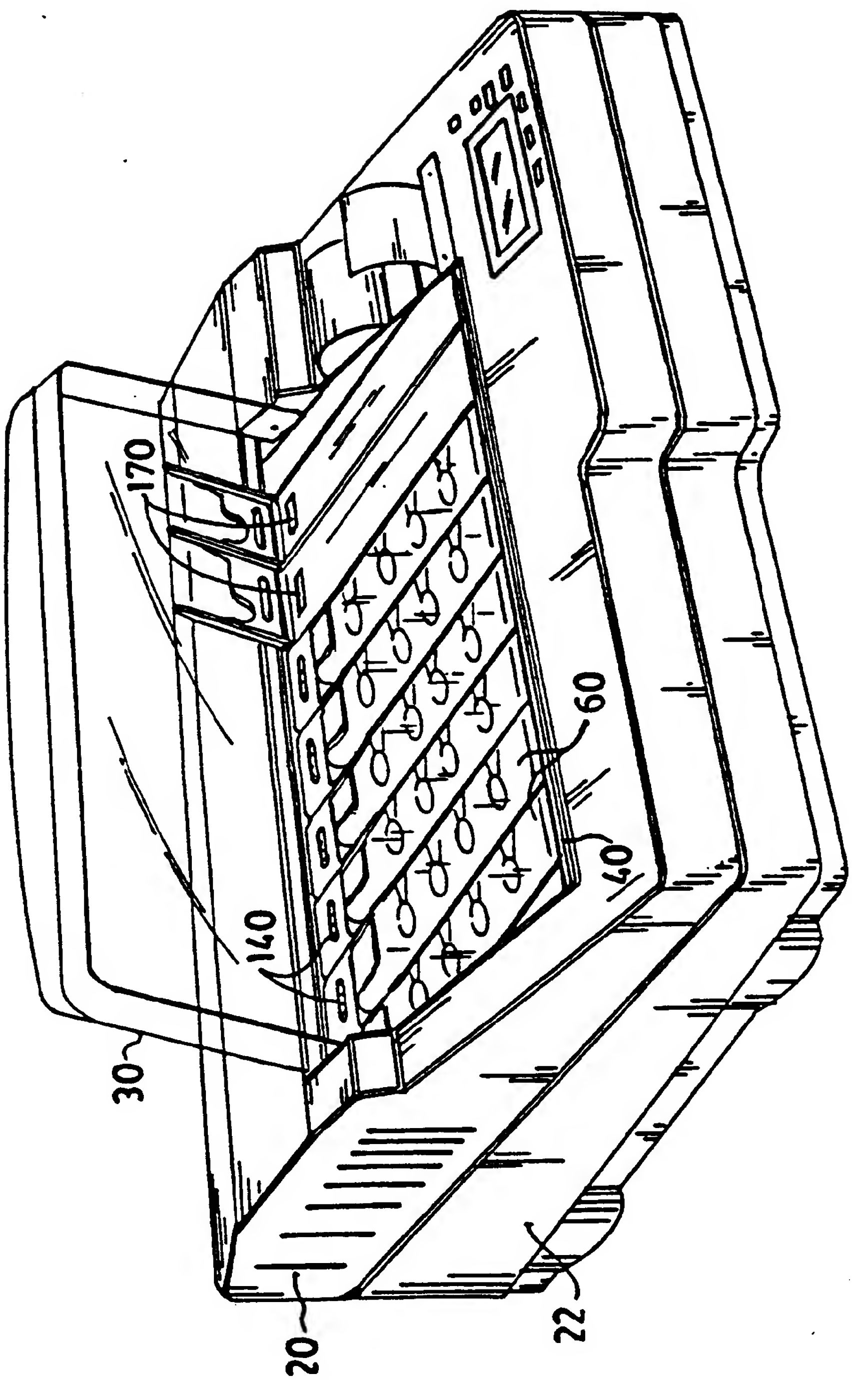


FIG.1

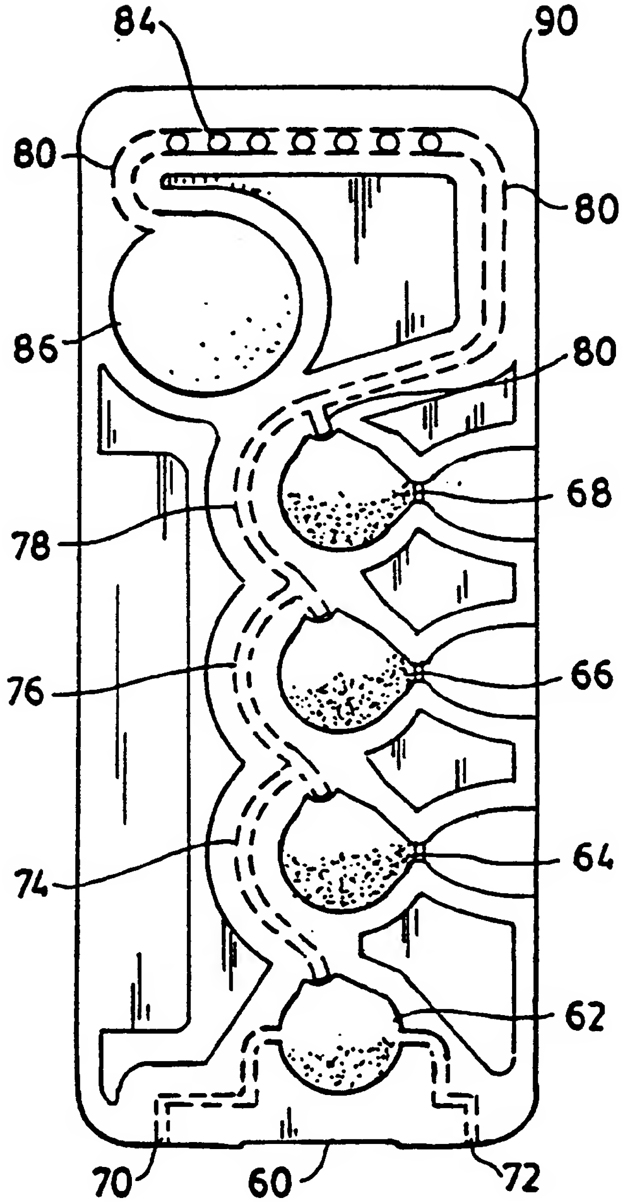


FIG. 2

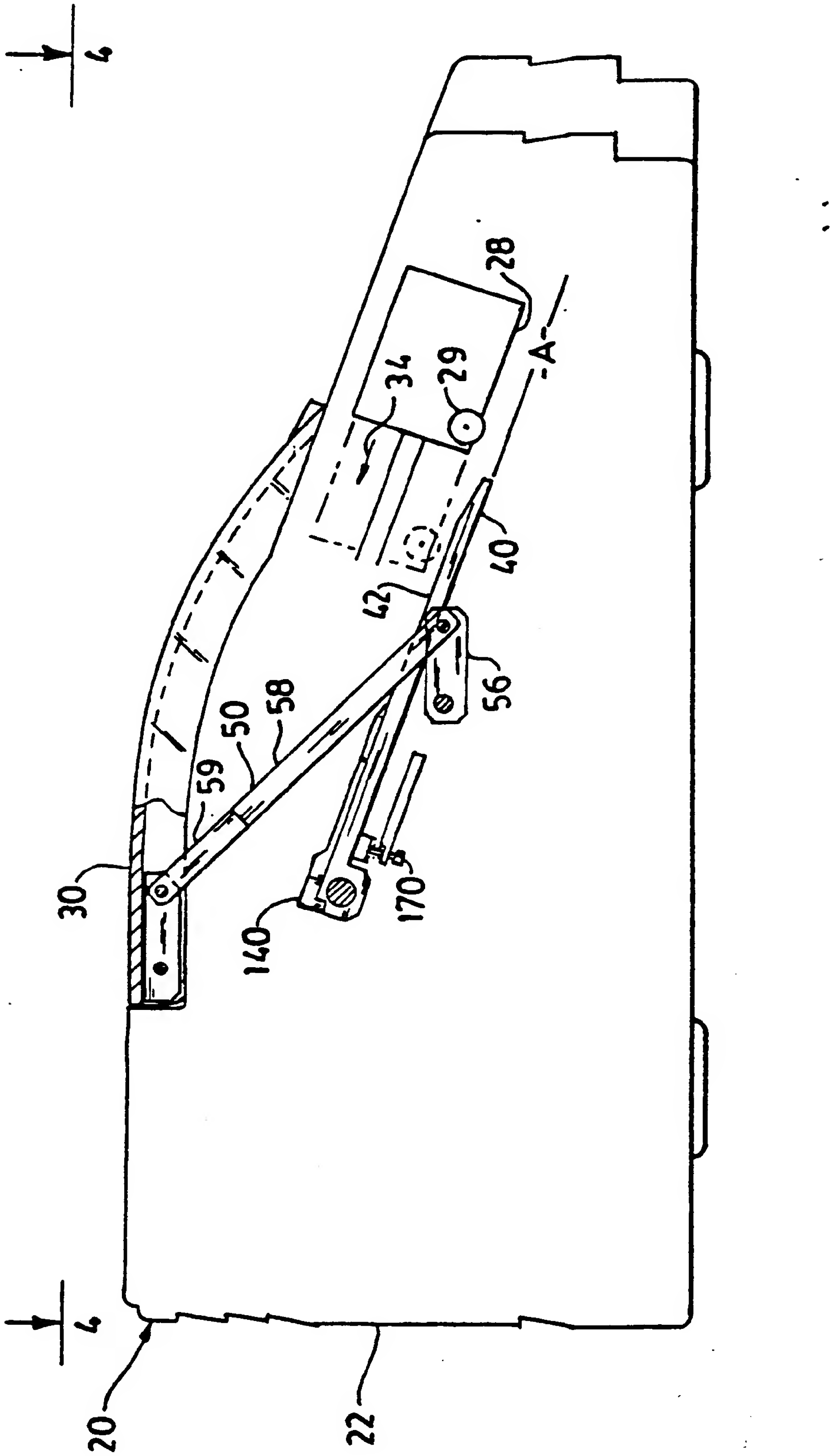


FIG. 3

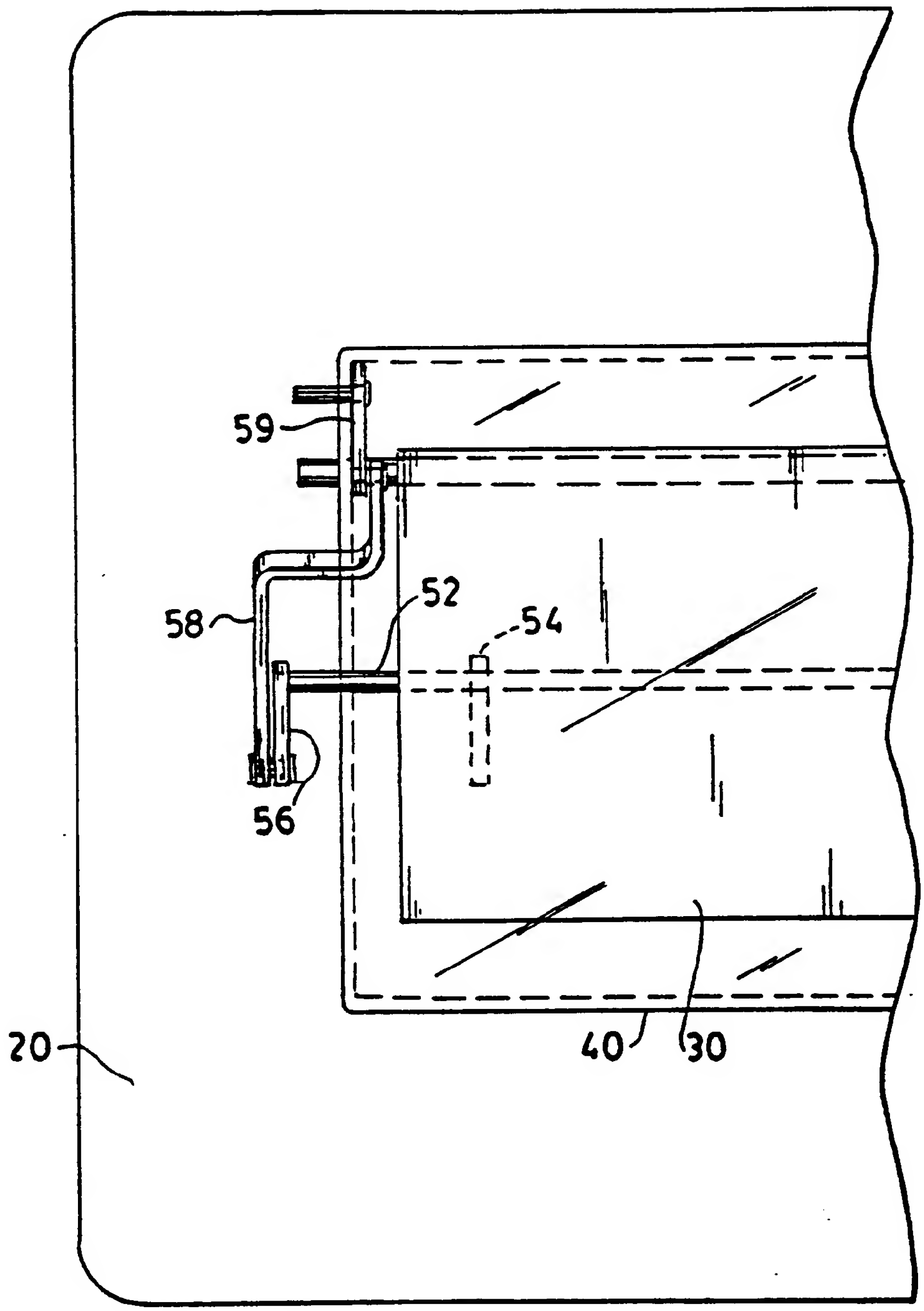


FIG.4

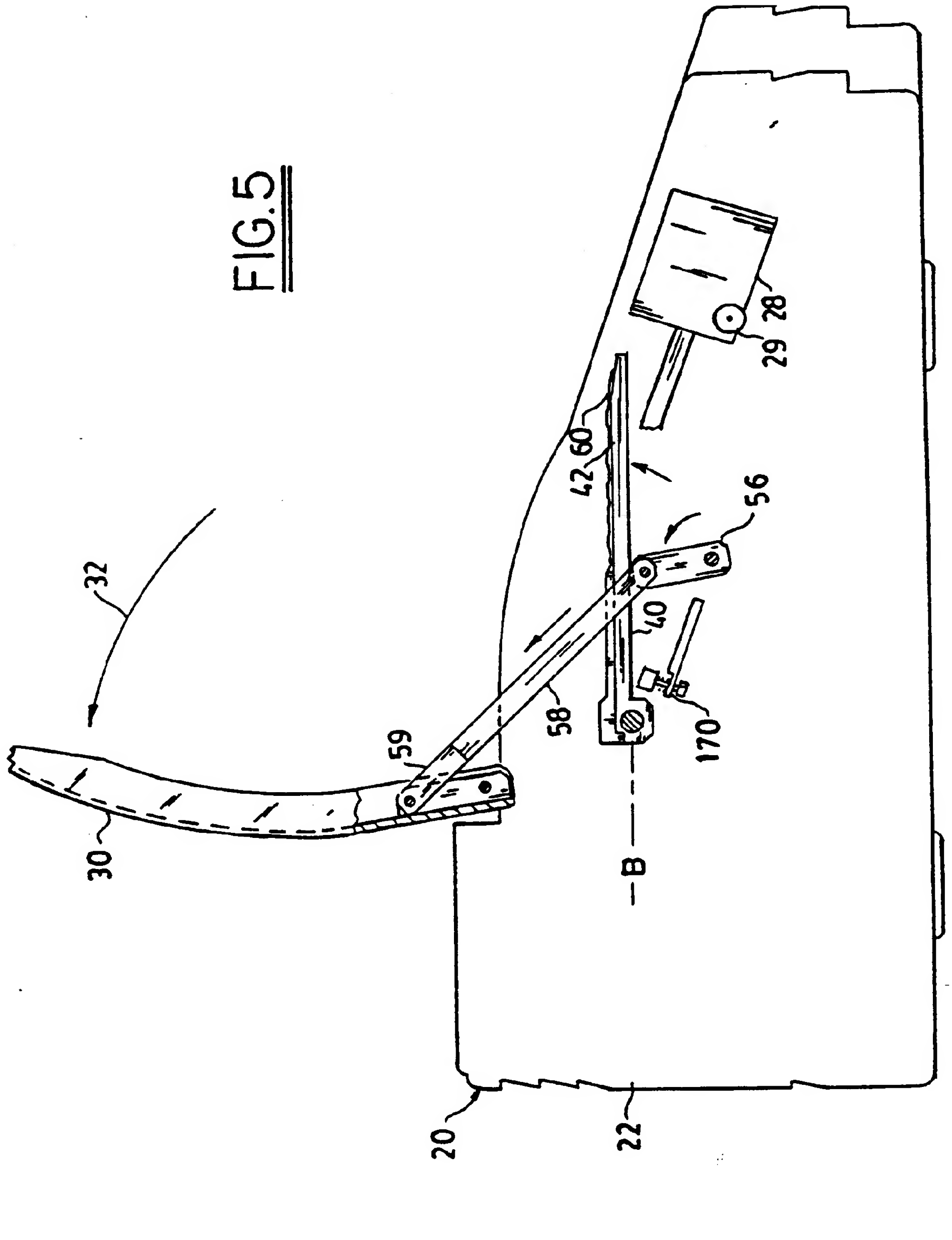
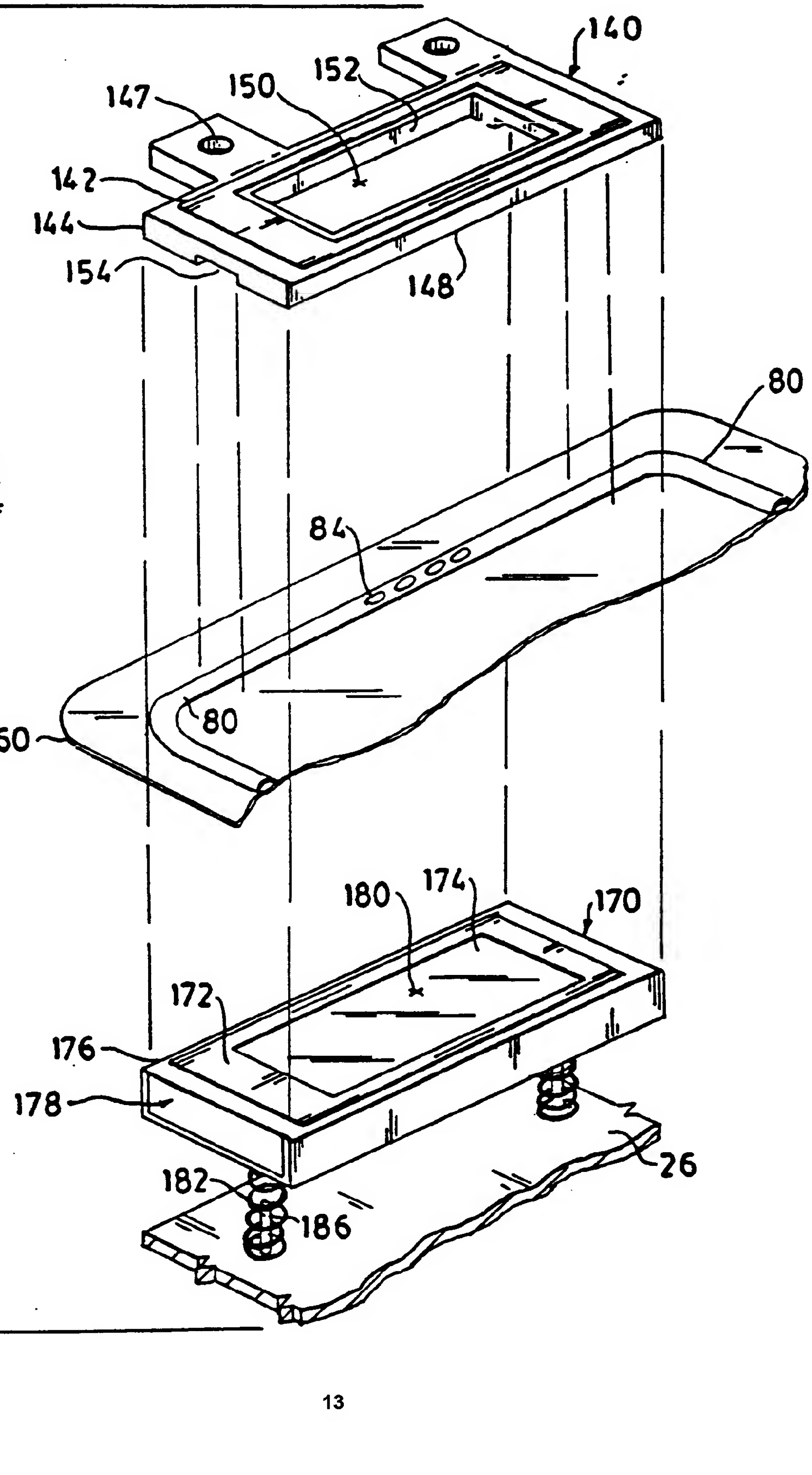


FIG.5



140
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FIG.6

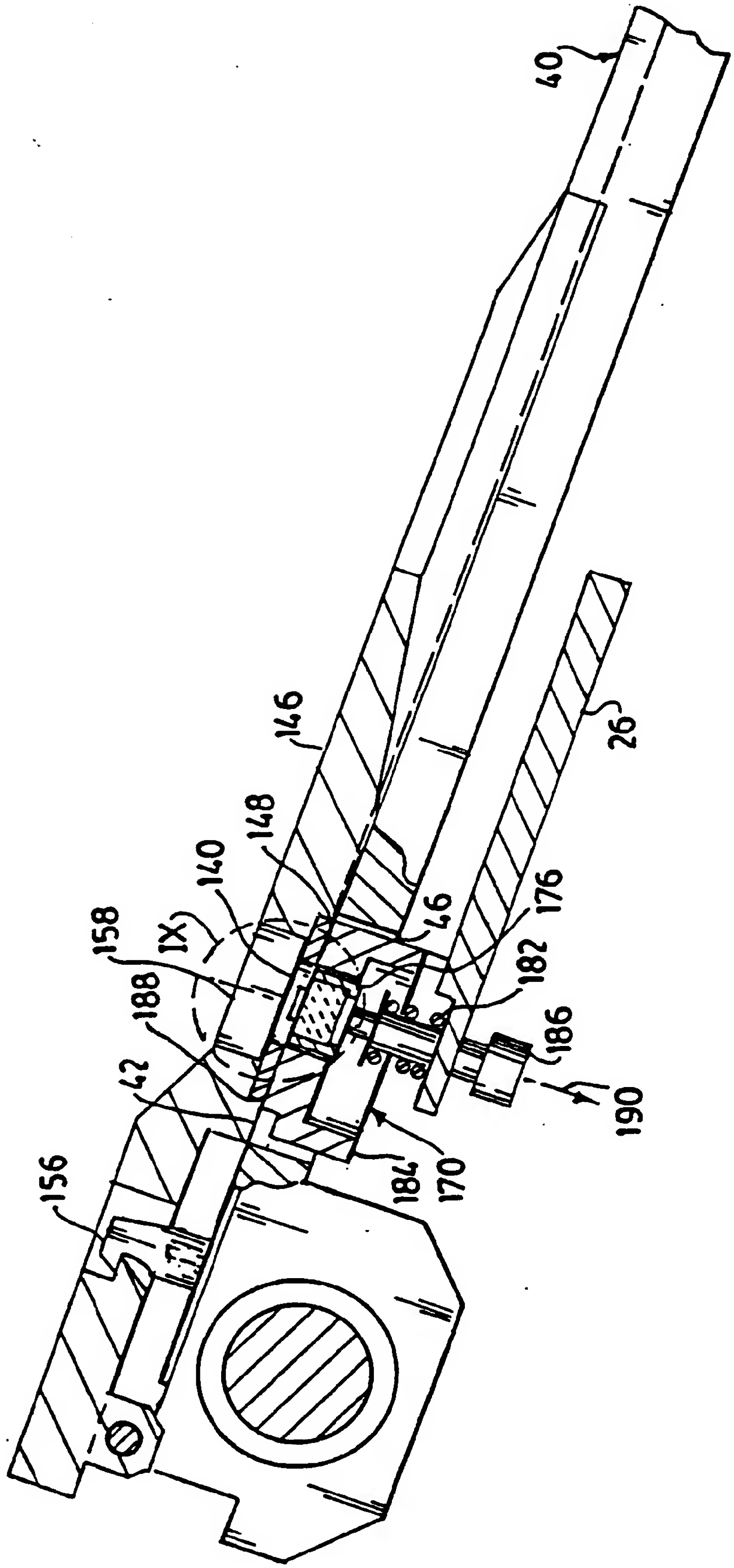

FIG.7

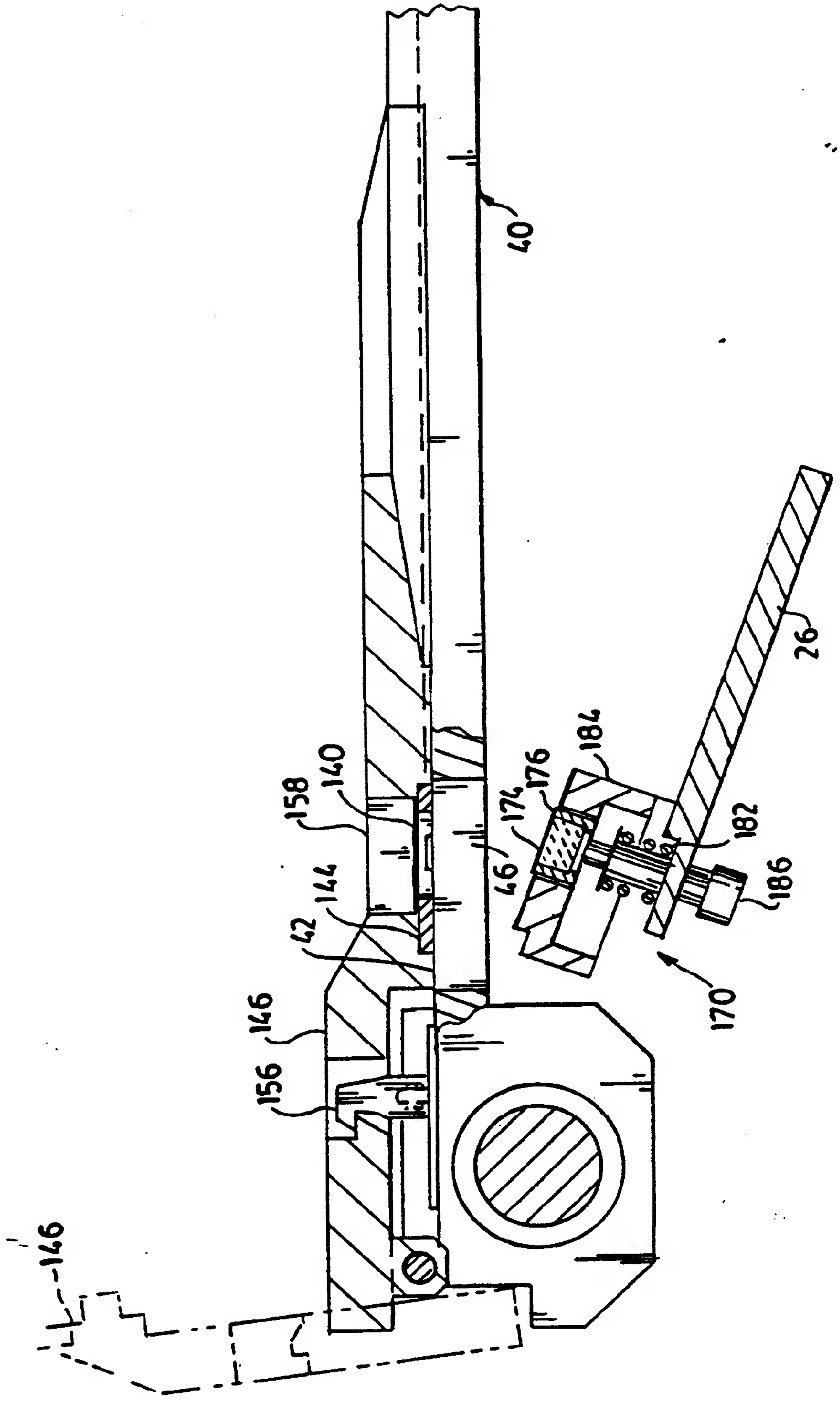

FIG.8

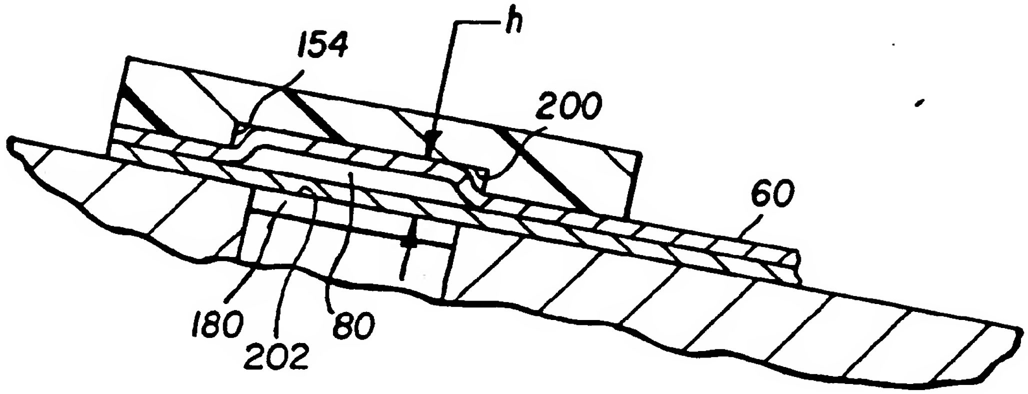

FIG. 9

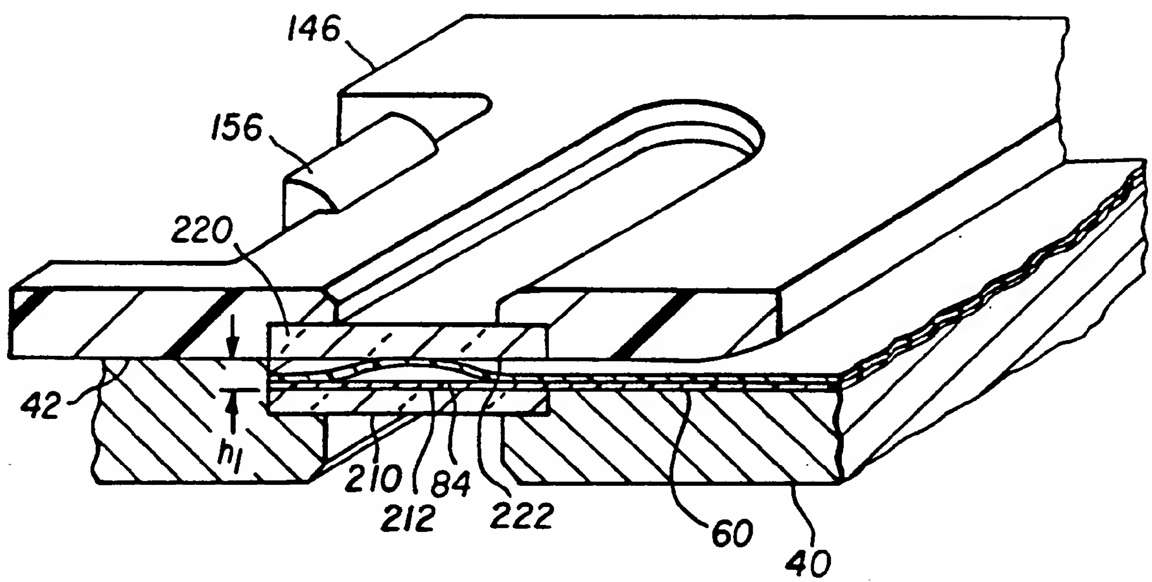

FIG. 10

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 95 30 0050

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	EP-A-0 402 994 (EASTMAN KODAK) * column 6, line 5 - line 43; figure 5 * ---	1,4,5,10	B01L7/00
A	US-A-4 038 030 (ALBRIGHT) * column 1, line 36 - line 45; figures * * column 6, line 56 - column 7, line 43 * * column 8, line 3 - line 49; figure 14 * ---	1,2,4,7	
A	US-A-5 241 415 (ARGENTIERI) * column 2, line 61 - column 3, line 14; figure 1 * * column 3, line 58 - column 4, line 5 * ---	2,3,6, 12,18	
A	WO-A-93 19207 (GENE TEC CORP.) * page 8, line 27 - page 9, line 21; figure 5 * * page 11, line 13 - page 12, line 23; figure 5 * * page 18, line 16 - line 23; figure 11 * -----	1	

TECHNICAL FIELDS SEARCHED (Int.Cl.6)

B01L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	21 February 1995	Hocquet, A

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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T : theory or principle underlying the invention
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D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document